10/669,705 filed 09/25/2003
Hao Chen et al.
Reply to Office Action of 07/09/2007

<div align="center">

REMARKS/ARGUMENTS
</div>

Claims 1–8 and 38–41 are pending in the above-captioned application. Of these pending claims, claims 1–8, 38, 40, and 41 stand rejected, and claim 39 is withdrawn from consideration. With this paper, claims 1, 3, 5, 7, and 41 have been amended, and claim 39 has been canceled. No new matter was added with the amendment.

I.   Claims under examination

The Examiner has withdrawn claim 39 from further consideration pursuant to 37 C.F.R 1.142(b) as being drawn to a nonelected species. With this paper, Applicants have canceled claim 39. Claims 1–8, 38, 40, and 41 are identified as reading on the elected species.

II.   Priority

Applicants acknowledge the Examiner's finding that the prior-filed applications, 09/558,232 and 10/105,407, fail to provide adequate support or enablement for the limitation "reverse partitioning" in Applicants' previously presented claim 3. In the present paper, Applicants have amended claim 3 to recite "recursive" partitioning rather than "reverse" partitioning. The term "reverse" appeared in the claims as a result of a typographical error. Please note that support for the limitation of "recursive" partitioning can be found, for example, on page 16, lines 11–14, of the present application, and in Figure 9. Thus, no new matter has been added by the amendment of the claim. Applicants respectfully submit that the limitation of recursive partitioning also finds support in both of the prior-filed applications. For example, reference to recursive partitioning can be found on page 13, lines 19–21, of the 09/558,232 application as filed as well as in paragraph 0104 of the 10/105,407 application as published (US 2002-0187514 A1). A grant of priority to each of these prior-filed applications is respectfully requested.

III.   Claim rejections under 35 U.S.C. § 112, second paragraph

Claims 3 and 7 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Each of the Examiner's reasons for rejecting claims 3 and 7 have been addressed in the amendments made to the still-pending claims.

10/669,705 filed 09/25/2003
Hao Chen et al.
Reply to Office Action of 07/09/2007

As discussed above, claim 3 has been amended to recite the limitation of "recursive" partitioning rather than "reverse" partitioning. The term "recursive partitioning" is fully defined on page 16, lines 11–14, of the present application. Please note that the limitation "reverse parititioning" appeared in claim 41 as added by Applicants' previous response. The present paper corrects this limitation to "recursive partitioning."

Claim 7 has been amended to eliminate the extraneous word "the" from the claim. Applicants believe this eliminates the perceived grammatical error.

Applicants respectfully assert that with the above amendments, claims 3, 7, and 41 should be found to comply with the requirements of 35 U.S.C. § 112, second paragraph.

IV. <u>Claim rejection under 35 U.S.C. § 112, first paragraph</u>

Claim 3 was rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention at the time the application was filed. As discussed previously, claim 3 contained a typographical error in which the word "reverse" was erroneously substituted for the intended word "recursive." Claim 3 has been amended to correct the typographical error. Applicants respectfully assert that with this amendment, claim 3 should be found to comply with the requirements of 35 U.S.C. § 112, first paragraph.

V. <u>Claim Rejections under 35 U.S.C. § 101</u>

Claims 1–8, 38, 40, and 41 were rejected under 35 U.S.C. § 101 as allegedly being drawn to non-statutory subject matter for failing to produce a useful, tangible, and concrete result. The rejection of these claims is respectfully traversed.

As previously presented and currently amended, claims 1–8, 38, 40, and 41 produce a <u>useful</u> result. Independent claim 1 and its dependent claims 2–4 describe processes that select a smaller subset of compounds from the original "plurality of candidate compounds" that can be expected to have desired activities at two or more molecular targets. See, e.g., page 7, lines 11–15, of the present application. The benefits of isolating a smaller set of promising compounds from a large set of drug candidate compounds are discussed extensively throughout the specification. See, e.g., page 5, line 3, through page 6, line 2; page 13, lines 5–10; and page 17, lines 12–21 of the present application. Independent claim 5 and its dependent claims 6–

10/669,705 filed 09/25/2003
Hao Chen et al.
Reply to Office Action of 07/09/2007

8 and 38–41 describe processes that predict the potential side effects of a drug candidate early in the drug discovery process. The benefits of early identification of side effects are also discussed extensively throughout the specification. See, e.g., page 3 lines, 13–20; page 5, line 18, through page 6, line 12; and page 17, line 28, through page 18, line 3, of the present application.

As previously presented and currently amended, the methods of claims 1–8, 38, 40, and 41 produce useful results. Independent claim 1 and its dependent claims 2–4 describe processes that select a smaller subset of compounds from the original "plurality of candidate compounds" that can be expected to have desired activities at two or more molecular targets. See, e.g., page 7, lines 11–15, of the present application. The benefits of isolating a smaller set of promising compounds from a large set of drug candidate compounds are discussed extensively throughout the specification. See, e.g., page 5, line 3, through page 6, line 2; page 13, lines 5–10; and page 17, lines 12–21 of the present application.

Independent claim 5 and its dependent claims 6–8 and 38–41 describe processes that aid in predicting potential side effects of a drug candidate early in the drug discovery process. The benefits of early identification of side effects (i.e., undesired activities) are also discussed extensively throughout the specification. See, e.g., page 3, lines 13–20; page 5, line 18, through page 6, line 12; and page 17, line 28, through page 18, line 3, of the present application. Please note that claim 5 has been amended to replace the term "compound" with the term "drug candidate" in the determining step. This amendment simply conforms the terminology of the determining step with that of the representing step. Thus, no new matter has been added by the amendment.

The methods of amended claims 1–8, 38, 40, and 41 also produce <u>tangible</u> results. The Examiner stated in the third paragraph on page 5 of the present Office action that applicant could likely overcome the rejection under 35 U.S.C. § 101 by amending the claims to recite a step that outputs results of the method, thereby providing a real-world result. Applicants have amended independent claim 1 and 5 in accordance with the Examiner's suggestion. Claim 1 now recites the step "providing output specifying the identified candidate compounds," while independent claim 5 now recites the step "providing output based on the determination, the output specifying whether the compound does or does not contain the set of compound descriptors." Support for the step of providing output can be found, for example, on page 13, line 23, of the specification. Thus, no new matter is added with the amendment. Applicants

10/669,705 filed 09/25/2003
Hao Chen et al.
Reply to Office Action of 07/09/2007

respectfully submit that, with the above-described amendments, independent claims 1 and 5 now provide tangible results, as do claims 2–8, 38, 40, and 41, which depend from claims 1 and 5.

As previously presented and currently amended, the methods of claims 1–8, 38, 40, and 41 produce <u>concrete</u> (i.e., repeatable) results. Because the structural features of molecular targets and compounds are unchanging, and it is these structural features that determine the interactions between the targets and compounds, results based on these interactions will be the same each time a claimed method is repeated with the same database and the same candidate compound(s). Therefore, the methods of independent claims 1 and 5 and their dependent claims produce repeatable results.

Applicants respectfully submit that all of the pending claims are now drawn to statutory subject matter. Withdrawal of the rejection of claims 1–8, 38, 40, and 41 under 35 U.S.C. § 101 is, therefore, respectfully requested.

VI.   Claim rejections under 35 U.S.C. § 102(b) as being anticipated by Nilakantan et al. (J. Chem. Inf. Comput. Sci.)

Claims 1, 2, 4–7, and 40 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Nilakantan et al. (J. Chem. Inf. Comput. Sci., 1993, Vol. 33, pp. 79–85). This rejection is respectfully traversed. "[F]or anticipation under 35 U.S.C. 102, the reference must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present." MPEP §§ 706.02 and 2131. "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, USPQ2d 1913, 1920 (Fed. Cir. 1989).

With respect to independent claims 1 and 5, at a minimum, Nilakantan et al. do not teach "providing a full-rank database of interactions between a plurality of molecular targets and a plurality of compounds" and "analyzing the database to identify a set of compound descriptors" associated with a) a set of desired interactions with two or more molecular targets (in claim 1) or b) both a desired activity and the absence of an undesired activity (in claim 5).

Specifically, Nilakantan et al. do not teach either creating or using (i.e., analyzing) a "full-rank" database. As described throughout Applicants' specification, a "full-rank" database must contain both positive and negative data. In other words, the database must record both the presence <u>and absence</u> of interactions between molecular targets and compounds.

10/669,705 filed 09/25/2003
Hao Chen et al.
Reply to Office Action of 07/09/2007

See, for example, the present application on page 15, lines 21–23; page 19 lines 24 and 25, through page 20, line 2; page 20, lines 25–27; page 23, lines 1–15; page 37, lines 18–29; as well as the limitation of original claim 32. As Applicants state on page 23, lines 12 and 13, "The core innovation and novelty is the use of the arrays of both positive and negative data in combination."

      Nilakantan et al. teach "a rapid technique to characterize molecular shapes without having to examine hundreds or thousands of docking orientations." See page 79, the bottom of column 1, continuing on to the top of column 2. Using this technique, Nilakantan et al. "compare a molecule with an entire database of candidates" (page 79, column 2, the fifth full paragraph), but then eliminate negative data (i.e., data regarding negative interactions) from the databases that result from this testing. For example, on page 80, column 1, at the beginning of the fourth full paragraph, Nilakantan et al. state (emphasis added), "The method could be used to screen large databases to eliminate those candidates which have a low shape similarity with the template." On page 80, column 1, at the end of the fifth full paragraph, Nilakantan et al. state (emphasis added), "We kept the 81 best-scoring compounds for further analysis." I.e., the negative data was lost. See, also, page 80, column 2, first full paragraph, "simply taking the highest scoring compounds"; page 80, column 2, near the end of the second full paragraph, "We … picked out structures … showing a high degree of shape match"; page 81, column 1, second complete paragraph, "simply screen the candidates ranked highest by the triplet method in the appropriate biological assay"; and page 84, column 2, at the end of the sixth full paragraph, "If this component had between 10 and 50 atoms, we kept it; otherwise we discarded it."

      Nothing in the teachings of Nilakantan et al. suggests creating and using a database that records both the presence and absence of interactions between molecular targets and compounds. The Examiner references Figs. 3 and 4 of Nilakantan et al., stating, "Candidate compounds are ranked and represented in terms of descriptors" by Nilakantan et al. Applicants respectfully direct the Examiner to page 80, column 2, at the end of the second full paragraph (emphasis added), "We experimented with the triplet method using the bound netropsin structure as the template and picked out structures (from a database of 22,498 compounds, which included the 10 best scoring compounds obtained by Grootenhuis) showing a high degree of shape match." Figs. 3 and 4 show only compounds ranked high by the triplet method. Thus, these are all examples of positive interaction data. Nilakantan et al. consistently teach selecting out only

10/669,705 filed 09/25/2003
Hao Chen et al.
Reply to Office Action of 07/09/2007

the <u>positive</u> interaction data. They do not teach or suggest maintaining interaction data for the low ranking compounds (<u>negative</u> data) along with the positive data in a full-rank database.

Thus, Nilakantan et al. do not teach every aspect of independent claims 1 and 5 either explicitly or impliedly, nor is the feature of a "full-rank" database inherently present in their teachings. Further, they do not show the identical invention claimed by Applicants in as complete detail as is contained in independent claims 1 and 5. Therefore, withdrawal of the rejection of independent claims 1 and 5 under § 102(b) as being anticipated by Nilakantan et al. is respectfully requested.

Claims 2 and 4 depend directly from amended independent claim 1, while claims 6, 7, and 40 depend directly from amended independent claim 5. Applicants respectfully submit that these dependent claims are allowable for at least the same reasons as set forth herein with respect to amended independent claims 1 and 5. Withdrawal of the rejection of dependent claims 2, 4, 6, 7, and 40 under § 102(b) as being anticipated by Nilakantan et al. is also respectfully requested.

VII. <u>Claim rejections under 35 U.S.C. § 103(a) as being made obvious by Nilakantan et al. (J. Chem. Inf. Comput. Sci.) in view of Chen et al. (J. Chem. Inf. Comput. Sci.) and Grass et al. (US 6,543,858)</u>

Claims 1–8, 38, 40, and 41 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nilakantan et al. (J. Chem. Inf. Comput. Sci., 1993, Vol. 33, pp. 79–85) as applied to claims 1, 2, 4–7, and 40, above, in view of Chen et al. (J. Chem. Inf. Comput. Sci., 1998, Vol. 38, pp. 1054–1062) and Grass et al. (US 6,543,858). The rejection of these claims is respectfully traversed.

To warrant rejection under 35 U.S.C. § 103(a), all the claim limitations must be taught or suggested by the prior art. MPEP § 2142. As demonstrated above, Nilakantan et al. neither teach nor suggest all of the limitations of Applicants' amended independent claims 1 and 5. Further, Applicants have demonstrated that Nilakantan et al. specifically teach away from Applicants' claimed full-rank database. Thus, amended independent claims 1 and 5 are nonobvious over the Nilakantan et al. reference. Any claim depending from a nonobvious claim is also nonobvious. MPEP § 2143.03 and *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Claims 2–4 depend directly from amended independent claim 1, while claims 6–8, 38,

10/669,705 filed 09/25/2003
Hao Chen et al.
Reply to Office Action of 07/09/2007

40, and 41 depend directly from amended independent claim 5. Therefore, dependent claims 2–4,

6–8, 38, 40, and 41 are nonobvious over the Nilakantan et al. reference.

The Examiner does not allege that Chen et al. teach all of the limitations recited in Applicants' independent claims 1 and 5, citing Chen et al. with reference only to dependent claims 3 and 41. However, the Examiner observes that Chen et al. "provide a database comprising active and inactive 3-D compound conformations." In the interest of avoiding any possible confusion, Applicants wish to point out that the cited database of Chen et al. is not the same as Applicants' claimed database because the database of Chen et al. includes only active and inactive <u>conformations</u>, while Applicants' claimed full-rank database comprises <u>interactions</u>. Chen et al. teach away from a full-rank database of <u>interactions</u> on page 1055, first column, first full paragraph, when they state, "we hoped that the following RP analyses could identify these active conformations from the inactive ones." I.e., they were concerned with isolating the positive interaction data from the negative interaction data. Nothing in Chen et al. suggests maintaining this negative interaction data along with the positive interaction data in a full-rank database. Therefore, amended independent claims 1 and 5 are nonobvious over the combination of Chen et al. and Nilakantan et al. Claim 3 depends directly from amended independent claim 1, while claim 41 depends directly from amended independent claim 5. As any claim depending from a nonobvious claim is also nonobvious, dependent claims 3 and 41 are nonobvious over the combination of Chen et al. and Nilakantan et al.

The Examiner cites Grass et al. with reference to Applicants' dependent claims 8 and 38. The Examiner has not alleged that Grass et al. teach the limitations demonstrated above to be absent from the Nilakantan et al. and Chen et al. references with respect to Applicants' amended independent claims 1 and 5, nor do Grass et al. do so. Therefore, amended independent claims 1 and 5 are nonobvious over Grass et al. alone or in any combination with Nilakantan et al. and Chen et al. Claims 8 and 38 depend directly from amended independent claim 5. As any claim depending from a nonobvious claim is also nonobvious, dependent claims 8 and 38 are nonobvious over the combination of Grass et al., Nilakantan et al., and Chen et al.

As demonstrated above, all of Applicants' claims 1–8, 38, 40, and 41 are nonobvious over Nilakantan et al. in view of Chen et al. and Grass et al. Withdrawal of the rejection of these claims under 35 U.S.C. § 103(a) is, therefore, respectfully requested.

10/669,705 filed 09/25/2003
Hao Chen et al.
Reply to Office Action of 07/09/2007

Conclusion

For the foregoing reasons, Applicants believe all the pending claims are in condition for allowance and should be passed to issue. If the Examiner believes that a telephone interview would expedite the examination of this application, the Examiner is requested to contact the undersigned attorney at the telephone number provided below.

Respectfully submitted,

/Ann C. Petersen/

Ann C. Petersen
Reg. No. 55,536

CARDINAL LAW GROUP
1603 Orrington Avenue, Suite 2000
Evanston, IL 60201
Direct: 408-223-2718
Fax: 847-905-7113
ann.petersen@cardinallawgroup.com